=> d his

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                DEL HIS Y
                ACT  DSULLIVAN/A
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L1              STR
L2              SCR 1192
L3         2560 SEA FILE=REGISTRY SSS FUL L2 AND L1
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     FILE 'HCAPLUS' ENTERED AT 09:24:38 ON 30 MAY 2002
L4          1535 S L3
L5          4264 S GENETIC (L) TRANSDUC?
L6         14147 S  RAAV OR ADENOVIRUS? OR ADENO (L) VIRUS?
L7            12 S L4 AND L6
L8             3 S L4 AND L5
L9            13 S L7 OR L8
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DICTIONARY FILE UPDATES:  28 MAY 2002  HIGHEST RN 422506-41-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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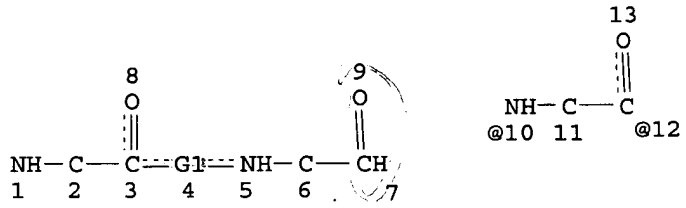


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L2                SCR 1192
L3          2560 SEA FILE=REGISTRY SSS FUL L2 AND L1

100.0% PROCESSED  10812 ITERATIONS                    2560 ANSWERS
SEARCH TIME: 00.00.02


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FILE 'HCAPLUS' ENTERED AT 09:25:56 ON 30 MAY 2002
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FILE COVERS 1907 - 30 May 2002 VOL 136 ISS 22
FILE LAST UPDATED: 28 May 2002 (20020528/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his l4-

FILE 'HCAPLUS' ENTERED AT 09:24:38 ON 30 MAY 2002
L4 1535 S L3
L5 4264 S GENETIC (L) TRANSDUC?
L6 14147 S RAAV OR ADENOVIRUS? OR ADENO (L) VIRUS?
L7 12 S L4 AND L6
L8 3 S L4 AND L5
L9 13 S L7 OR L8

=> d .ca hitstr l9 1-13

L9 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:126971 HCAPLUS
DOCUMENT NUMBER: 136:323078
TITLE: Expression of herpes simplex virus ICP0 inhibits the induction of interferon-stimulated genes by viral infection
AUTHOR(S): Eidson, Kasey M.; Hobbs, William E.; Manning, Brian J.; Carlson, Paul; DeLuca, Neal A.
CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261, USA
SOURCE: Journal of Virology (2002), 76(5), 2180-2191
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The herpes simplex virus type 1 (HSV-1) mutant d109 does not express any of the immediate-early (IE) proteins and persists in cells for a prolonged length of time. As has been shown by Nicholl et al. and Mossman et al. using other mutants defective for IE gene expression, infection with d109 induced the expression of a no. of interferon-stimulated genes. Induction of these genes was significantly greater at multiplicities of infection (MOI) of 10 PFU/cell or greater, and the resulting antiviral effect was only seen at MOIs greater than 10 PFU/cell. Using mutants defective for sets of IE genes established that the lack of ICP0 expression was

necessary for high levels of interferon-stimulated gene expression in HEL cells. The induction of interferon-stimulated genes by d109 could also be inhibited by infection with an E1-:E3-:E4- adenovirus expressing levels of ICP0 that are comparable to those expressed within the first hour of wild-type virus infection. Lastly, the addn. of the proteasome inhibitor MG132 to cells infected with a mutant that expresses ICP0, d106, also resulted in the induction of interferon-stimulated genes. Thus, ICP0 may function through the proteasome very early in HSV infection to inhibit a cellular antiviral response induced by the virion.

CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 10

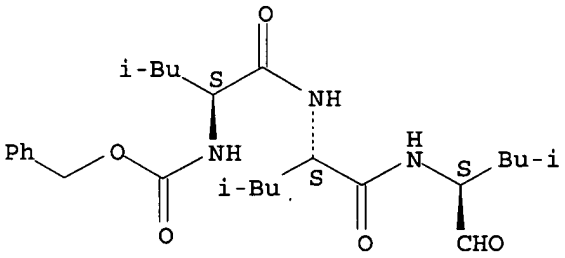
IT Human
Human **adenovirus**
Human herpesvirus 1
(expression of herpes simplex virus ICP0 inhibits the induction of interferon-stimulated genes by viral infection)

IT **133407-82-6**, MG132 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression of herpes simplex virus ICP0 inhibits the induction of interferon-stimulated genes by viral infection)

IT **133407-82-6**, MG132
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression of herpes simplex virus ICP0 inhibits the induction of interferon-stimulated genes by viral infection)

RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:126958 HCAPLUS
DOCUMENT NUMBER: 136:321814
TITLE: Ubiquitination of both **adeno**-associated **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors
AUTHOR(S): Yan, Ziying; Zak, Roman; Luxton, G. W. Gant; Ritchie, Teresa C.; Bantel-Schaal, Ursula; Engelhardt, John F.
CORPORATE SOURCE: Department of Anatomy and Cell Biology, and Center for Gene Therapy, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of Virology (2002), 76(5), 2043-2053
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the presence of complementing adeno-assocd. virus type 2 (AAV-2) Rep proteins, AAV-2 genomes can be pseudotyped with the AAV-5 capsid to assemble infectious virions. Using this pseudotyping strategy, the involvement of the ubiquitin-proteasome system in AAV-5 and AAV-2 capsid-mediated infections was compared. A recombinant AAV-2 (rAAV-2) proviral luciferase construct was packaged into both AAV-2 and AAV-5 capsid particles, and transduction efficiencies in a no. of cell lines were compared. Using luciferase expression as the end point, we demonstrated that coadministration of the viruses with proteasome inhibitors not only increased the transduction efficiency of rAAV-2, as previously reported, but also augmented rAAV-5-mediated gene transfer. Increased transgene expression was independent of viral genome stability, since there was no significant difference in the amts. of internalized viral DNA in the presence or absence of proteasome inhibitors. Western blot assays of immunopptd. viral capsid proteins from infected HeLa cell lysates and in vitro reconstitution expts. revealed evidence for ubiquitin conjugation of both AAV-2 and AAV-5 capsids. Interestingly, heat-denatured virus particles were preferential substrates for in vitro ubiquitination, suggesting that endosomal processing of the viral capsid proteins is a prelude to ubiquitination. Furthermore, ubiquitination may be a signal for processing of the capsid at the time of virion disassembly. These studies suggest that the previously reported influences of the ubiquitin-proteasome system on rAAV-2 transduction are also active for rAAV-5 and provide a clearer mechanistic framework for understanding the functional significance of ubiquitination.

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1, 14

ST ubiquitination capsid protein transduction efficiency recombinant **adeno** assocd **virus**

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(capsid; ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors)

IT DNA formation factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene rep; ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors)

IT **Adeno**-associated **virus** 2
Adeno-associated **virus** 5
Post-translational processing
Transduction, genetic
(ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the **transduction** efficiency of recombinant vectors)

IT Infection
(viral; ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors)

IT 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors)

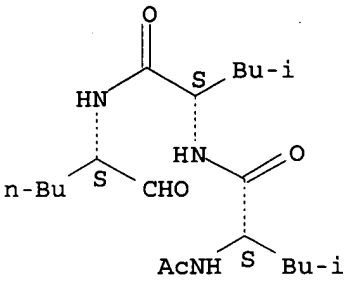
IT **110044-82-1 133407-82-6**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of

recombinant vectors)

IT **110044-82-1 133407-82-6**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ubiquitination of both **adeno**-assocd. **virus** type 2 and 5 capsid proteins affects the transduction efficiency of recombinant vectors)

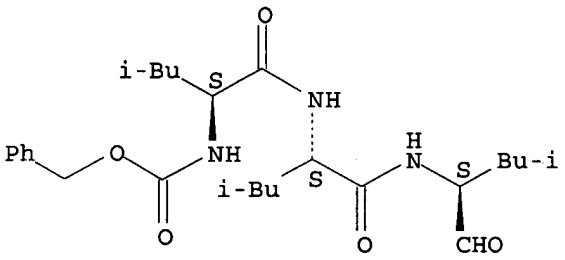
RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:188924 HCAPLUS
DOCUMENT NUMBER: 135:13799
TITLE: Use of short-lived green fluorescent protein for the detection of proteasome inhibition
AUTHOR(S): Andreatta, C.; Nahreini, P.; Hovland, A. R.; Kumar, B.; Edwards-Prasad, J.; Prasad, K. N.
CORPORATE SOURCE: University of Colorado Health Sciences Center, Denver, CO, USA
SOURCE: BioTechniques (2001), 30(3), 656-660
CODEN: BTNQDO; ISSN: 0736-6205
PUBLISHER: Eaton Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human embryonic kidney (HEK293) cells were stably transduced with a

retroviral vector contg. an expression cassette for a short-lived green fluorescent protein (d2EGFP) and the neomycin resistance gene (Neor). When Neor HEK293 clones were treated with proteasome inhibitors, lactacystin or MG132, an increase in the constitutive levels of d2EGFP expression was obsd. Based on flow cytometry, proteasome inhibitors induced a 5- to 10-fold increase in the fluorescent intensity of d2EGFP in HEK293 cell clones. However, in the presence of proteasome inhibitors, HEK293 clones showed a 4- to 6.5-fold increase in d2EGFP concn. as detd. by western blot anal. Our data suggest that d2EGFP is a useful indicator of proteasome inhibition. Therefore, stable expression of d2EGFP in mammalian cells is potentially useful for high-throughput screening of cDNAs or pharmaceutical drugs that repress proteasome functions in vivo.

CC 1-1 (Pharmacology)
Section cross-reference(s): 9

IT **Transduction, genetic**
(use of short-lived green fluorescent protein for detection of proteasome inhibition)

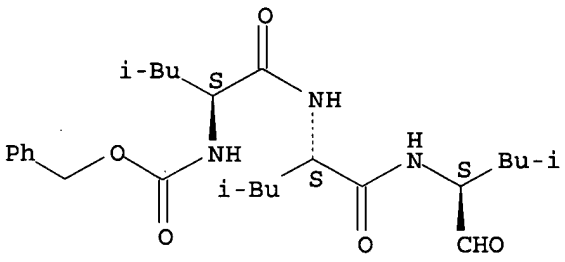
IT 133343-34-7, Lactacystin **133407-82-6**, MG132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(use of short-lived green fluorescent protein for detection of proteasome inhibition)

IT **133407-82-6**, MG132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(use of short-lived green fluorescent protein for detection of proteasome inhibition)

RN 133407-82-6 HCAPLUS

CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:100410 HCAPLUS

DOCUMENT NUMBER: 135:222015

TITLE: Intracellular trafficking of **adeno**-associated **virus** vectors: routing to the late endosomal compartment and proteasome degradation

AUTHOR(S): Douar, Anne-Marie; Poulard, Karine; Stockholm, Daniel; Danos, Olivier

CORPORATE SOURCE: Genethon III-CNRS URA 1923, Evry, F-91002, Fr.

SOURCE: Journal of Virology (2001), 75(4), 1824-1833
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The early steps of adeno-assocd. virus (AAV) infection involve attachment to a variety of cell surface receptors (heparan sulfate, integrins, and fibroblast growth factor receptor 1) followed by clathrin-dependent or independent internalization. Here the authors have studied the subsequent intracellular trafficking of AAV particles from the endosomal compartment to the nucleus. Human cell lines were transduced with a recombinant AAV (rAAV) carrying a reporter gene (luciferase or green fluorescent protein) in the presence of agents that affect trafficking. The effects of bafilomycin A1, brefeldin A, and MG-132 were measured. These drugs act at the level of endosome acidification, early-to-late endosome transition, and proteasome activity, resp. The authors obsd. that the transducing virions needed to be routed as far as the late endosomal compartment. This behavior was markedly different from that obsd. with adenovirus particles. Antiproteasome treatments with MG-132 led to a 50-fold enhancement in transduction efficiency. This effect was accompanied by a 10-fold intracellular accumulation of single-stranded DNA AAV genomes, suggesting that the mechanism of transduction enhancement was different from the one mediated by a helper adenovirus, which facilitates the conversion of the rAAV single-stranded DNA genome into its replicative form. MG-132, a drug currently in clin. use, could be of practical use for potentializing rAAV-mediated delivery of therapeutic genes.

CC 3-2 (Biochemical Genetics)

ST **adeno** assocd **virus** vector transport endosome nucleus

IT Organelle
(endocytic vesicle; intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV**-mediated delivery of therapeutic genes)

IT **Adeno**-associated **virus**
Cell nucleus
Gene therapy
Transformation, genetic
Virus vectors
(intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV**-mediated delivery of therapeutic genes)

IT Biological transport
(intracellular; intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV**-mediated delivery of therapeutic genes)

IT 20350-15-6, Brefeldin A 88899-55-2, Bafilomycin A1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV**-mediated delivery of therapeutic genes)

IT **133407-82-6**, MG-132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV**-mediated delivery of therapeutic genes)

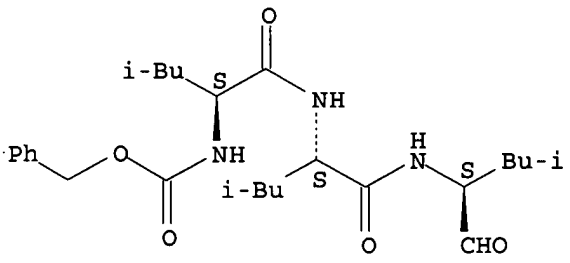
IT 140879-24-9, Proteasome

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV** -mediated delivery of therapeutic genes)

IT **133407-82-6**, MG-132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intracellular trafficking of **adeno**-assocd. **virus** vectors from endosomal compartment to nucleus and effect of drugs on proteasome activity in relation to potentializing **rAAV** -mediated delivery of therapeutic genes)

RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:881351 HCAPLUS
DOCUMENT NUMBER: 134:46764
TITLE: Compounds and methods to enhance recombinant **adeno**-associated **virus** (**rAAV**) transduction for gene therapy
INVENTOR(S): Engelhardt, John F.; Duan, Dongsheng
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075365	A2	20001214	WO 2000-US15700	20000608
WO 2000075365	A3	20010301		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1190249 A2 20020327 EP 2000-944624 20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-138188P P 19990608
US 2000-201089P P 20000502
WO 2000-US15700 W 20000608
OTHER SOURCE(S): MARPAT 134:46764
AB Agents and methods to alter rAAV transduction are provided.
IC ICM C12Q001-00
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3, 8
ST adenoassociated virus **genetic** vector **transduction**
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E2 (ubiquitin-carrier) protein degrdn. factor; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT **Transduction, genetic**
UV radiation
Virus vectors
(compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) **transduction** for gene therapy)
IT Transgene
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Bronchi
Respiratory tract
(epithelium; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Gene, microbial
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(marker; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Biological transport
(nuclear; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Endosome
(processing in; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Peptides, biological studies
Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(recombinant **virus** encoding; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Cell nucleus
(trafficking to; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for

gene therapy)
IT Dog (Canis familiaris)
Liver
Lung
Mammal (Mammalia)
Mouse
Rabbit
Rat
(transduction of cells of; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Fibroblast
(transduction of; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ubiquitin-conjugating, activation of; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT **Adeno**-associated **virus**
(vectors; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT Endocytosis
(viral; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT 60267-61-0, Ubiquitin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT 9001-78-9, Alkaline phosphatase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(airway epithelium and liver expression of; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT 54-05-7, Chloroquine 67-42-5, Egta 7298-84-2 14930-96-2, Cytochalasin b 16874-75-2, L-Alanine, L-histidyl- 20350-15-6, Brefeldin a 31430-18-9, Nocodazole **133407-82-6** 148333-42-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT 146397-20-8, Cy3
RL: RCT (Reactant); RACT (Reactant or reagent)
(compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)
IT 3654-96-4, L-Methionine-35S
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(compds. and methods to enhance recombinant **adeno**-assocd.

virus (**rAAV**) transduction for gene therapy)

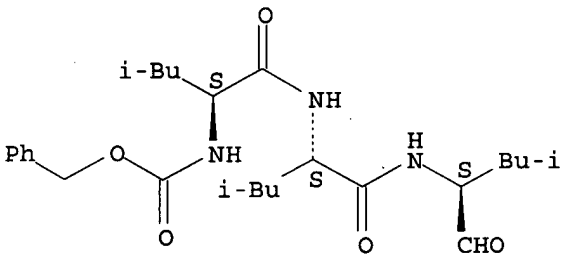
IT 37205-61-1, Proteinase inhibitor
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(endosomal; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)

IT 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)

IT **133407-82-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and methods to enhance recombinant **adeno**-assocd. **virus** (**rAAV**) transduction for gene therapy)

RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:392015 HCAPLUS
DOCUMENT NUMBER: 133:114745
TITLE: Calpain inhibitor 1 activates p53-dependent apoptosis in tumor cell lines
AUTHOR(S): Atencio, Isabella A.; Ramachandra, Murali; Shabram, Paul; Demers, G. William
CORPORATE SOURCE: Canji, Inc., San Diego, CA, 92121, USA
SOURCE: Cell Growth & Differentiation (2000), 11(5), 247-253
CODEN: CGDIE7; ISSN: 1044-9523
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reports suggest a role of calpains in degrdn. of wild-type p53, which may regulate p53 induction of apoptosis. A calpain inhibitor, n-acetyl-leu-leu-norleucinal (calpain inhibitor 1), was assessed for ability to enhance p53-dependent apoptosis in human tumor cell lines with endogenous wild-type p53 and in altered p53 cell lines with the replacement of wild-type p53 by a recombinant adenovirus (rAd-p53). Calpain inhibitor 1 treatment resulted in increased levels of activated p53, increased p21 protein, and activation of caspases. Cell lines with wild-type, but not mutated or null, p53 status arrested in G0/G1 and were sensitive to calpain inhibitor-induced apoptosis. Regardless of

endogenous p53 status, calpain inhibitor treatment combined with rAd-p53, but not empty vector virus, enhanced apoptosis in tumor cell lines. These results demonstrate p53-dependent apoptosis induced by a calpain inhibitor and further suggest a role for calpains in the regulation of p53 activity and induction of apoptotic pathways.

CC 1-6 (Pharmacology)
Section cross-reference(s): 3

ST antitumor p53 apoptosis calpain inhibitor 1; anticancer gene therapy rAdp53 **adenovirus** vector

IT Antitumor agents
Apoptosis
Cytomegalovirus
Gene therapy
Human **adenovirus**
Signal transduction, biological
Virus vectors
(calpain inhibitor 1 activates p53-dependent apoptosis in tumor cell lines)

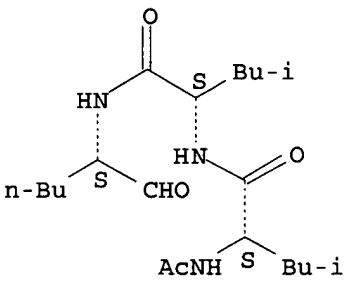
IT **110044-82-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calpain inhibitor 1 activates p53-dependent apoptosis in tumor cell lines)

IT **110044-82-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calpain inhibitor 1 activates p53-dependent apoptosis in tumor cell lines)

RN 110044-82-1 HCAPLUS

CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:391548 HCAPLUS

DOCUMENT NUMBER: 133:114878

TITLE: Endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-associated **virus**

AUTHOR(S): Duan, Dongsheng; Yue, Yongping; Yan, Ziying; Yang, Jusan; Engelhardt, John F.

CORPORATE SOURCE: Department of Anatomy and Cell Biology, Center for Gene Therapy, University of Iowa, Iowa City, IA, USA

SOURCE: Journal of Clinical Investigation (2000), 105(11), 1573-1587
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The restriction of viral receptors and coreceptors to the basolateral surface of airway epithelial cells has been blamed for the inefficient transfer of viral vectors to the apical surface of this tissue. We now report, however, that differentiated human airway epithelia internalize rAAV type-2 virus efficiently from their apical surfaces, despite the absence of known adeno-assocd. virus-2 (AAV-2) receptors or coreceptors at these sites. The dramatically lower transduction efficiency of rAAV infection from the apical surface of airway cells appears to result instead from differences in endosomal processing and nuclear trafficking of apically or basolaterally internalized virions. AAV capsid proteins are ubiquitinated after endocytosis, and gene transfer can be significantly enhanced by proteasome or ubiquitin ligase inhibitors. Tripeptide proteasome inhibitors increased persistent rAAV gene delivery from the apical surface >200-fold, to a level nearly equiv. to that achieved with basolateral infection. In vivo application of proteasome inhibitor in mouse lung augmented rAAV gene transfer from undetectable levels to a mean of 10.4 .+-. 1.6% of the epithelial cells in large bronchioles. Proteasome inhibitors also increased rAAV-2-mediated gene transfer to the liver tenfold, but they did not affect transduction of skeletal or cardiac muscle. These findings suggest that tissue-specific ubiquitination of viral capsid proteins interferes with rAAV-2 transduction and provides new approaches to circumvent this barrier for gene therapy of diseases such as cystic fibrosis.

CC 1-9 (Pharmacology)
Section cross-reference(s): 10, 63

IT Cell membrane
(apical; endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(capsid; endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

IT **Adeno**-associated **virus** 2
Cystic fibrosis
Drug delivery systems
Endocytosis
Endosome
Gene therapy
Liver
Muscle
(endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

IT Respiratory tract
(epithelium; endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

IT Biological transport
(internalization; endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

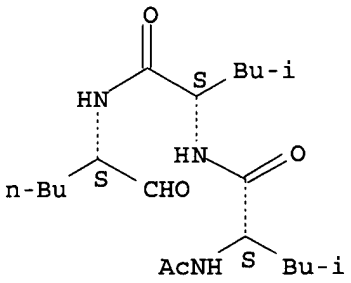
IT **110044-82-1**, Calpain inhibitor I **133407-82-6**, MG132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

IT **110044-82-1**, Calpain inhibitor I **133407-82-6**, MG132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(endosomal processing limits gene transfer to polarized airway epithelia by **adeno**-assocd. **virus**)

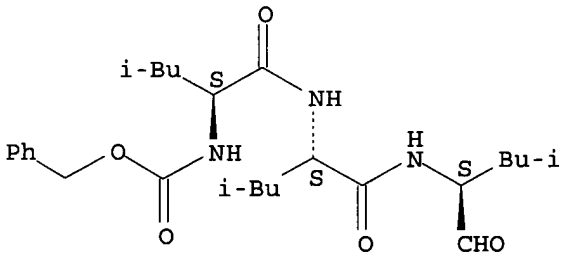
RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:351682 HCAPLUS
DOCUMENT NUMBER: 133:1514
TITLE: Recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy
INVENTOR(S): Wills, Kenneth N.
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029599	A1	20000525	WO 1999-US26004	19991117

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO,

NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1131458 A1 20010912 EP 1999-967094 19991117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO

PRIORITY APPLN. INFO.: US 1998-195367 A 19981118
WO 1999-US26004 W 19991117

AB Recombinant adenovirus vectors have constructed to express tumor suppressor gene p53 under the control of adenovirus (Ad) 5 major late promoter by replacing Ad 5 E1a and E1b coding sequences necessary for viral replication. These vectors are evaluated in vivo by testing p53 expression in MRC9 cells, SK-HEP1 cells, and NCI H358 cells. P53 indeed demonstrates temporal (later) and greater expression in vivo. These p53 recombinant adenoviral vectors are capable to replicate and lyse neoplastic cells, and time course of viral replication and therapeutic efficacy are also studied. Other adenoviral vectors are also constructed to express cytosine deaminase gene or interferon 2.alpha. (IFN2.alpha.) gene. The vectors may optionally include modifications in the viral genome so as to impart addnl. therapeutic, conditionally replicating or targeting functions. Methods to prep. and use these vectors, including pharmaceutical formulations are provided.

IC ICM C12N015-86
ICS C12N015-57; C07K014-47; A61K048-00; A61P035-00; C12N005-06; C12N005-10

CC 3-5 (Biochemical Genetics)
Section cross-reference(s): 1, 10, 13, 14

ST recombinant **adenovirus** viral vector p53 transcription regulation gene therapy; major late promoter **adenovirus** p53 transcription regulation

IT Gene, microbial
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(E1A, 12S or 13S; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Gene, microbial
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(E1B, 55K; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Gene, microbial
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(E4; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(TP53; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT .alpha.-Fetoproteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene of, promoter from; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Drug delivery systems
(injections, i.p.; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Drug delivery systems
(injections, i.v.; recombinant **adenovirus** vectors with late

transgene expression for cancer gene therapy)

IT Drug delivery systems
(intratumoral injection; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Promoter (genetic element)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(major late, **adenovirus** 5; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Promoter (genetic element)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of fetoprotein .alpha. gene; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Virus vectors
(recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Human **adenovirus** 5
(recombinant; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Cell
(stem, tumor elimination from; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(tumor suppressor; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT Interferons
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.alpha.2, gene for; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT **110044-82-1**, N-Acetyl-Leu-Leu-norleucinal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calpain inhibitor, as drug delivery enhancing agents; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

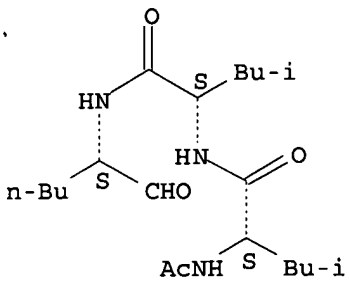
IT 9025-05-2, Cytosine deaminase
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gene for; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT 78990-62-2, Calpain
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of, as drug delivery enhancing agents; recombinant **adenovirus** vectors with late transgene expression for cancer gene therapy)

IT **110044-82-1**, N-Acetyl-Leu-Leu-norleucinal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calpain inhibitor, as drug delivery enhancing agents; recombinant **adenovirus** vectors with late transgene expression for cancer

gene therapy)
RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:351657 HCAPLUS
DOCUMENT NUMBER: 132:344118
TITLE: Adenoviral vectors with E1B deletion replicated in tumor cells and their use in cancer therapy
INVENTOR(S): Howe, John A.; Perry, Stuart T.
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

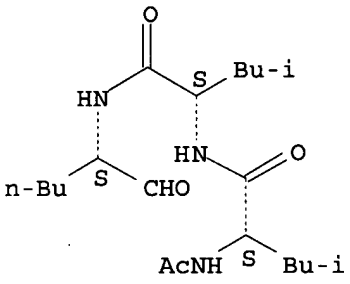
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029573	A2	20000525	WO 1999-US26003	19991117
WO 2000029573	A3	20001005		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-195748 A 19981118
AB The present invention provides a replication competent recombinant adenovirus contg. a constitutive viral or cellular promotor operably linked to a p53 gene, wherein said vector is defective in E1B55K function. The vectors of the present invention are capable of replication and lysis of neoplastic cells. The vectors may optionally include modifications to the genome so as to impart addnl. therapeutic or targeting functions. The present invention also provides pharmaceutical formulations of such vectors. The present invention further provides methods of use and prepg. of such vectors.
IC ICM C12N015-12
ICS C12N015-34; C12N015-861; C07K014-075; C07K014-47; A61K038-05;

A61K048-00; A61P035-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 10, 13
IT Human **adenovirus** 5
(recombinant, replication competent; adenoviral vectors with E1B deletion preferentially replicated in tumor cells and their use in cancer therapy)
IT **110044-82-1**
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Calpain inhibitor I, pharmaceutical formulation comprising; adenoviral vectors with E1B deletion preferentially replicated in tumor cells and their use in cancer therapy)
IT **110044-82-1**
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Calpain inhibitor I, pharmaceutical formulation comprising; adenoviral vectors with E1B deletion preferentially replicated in tumor cells and their use in cancer therapy)
RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:723196 HCAPLUS
DOCUMENT NUMBER: 131:333006
TITLE: Production of recombinant replication-deficient viral vectors encoding exogenous transgenes via microcarrier-based process
INVENTOR(S): Giroux, Daniel D.; Goudreau, Ann M.; Ramachandra, Muralidhara; Shabram, Paul W.
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957297	A1	19991111	WO 1999-US9813	19990504

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT,

RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, ZA,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 5994134	A	19991130	US 1998-73076	19980504	
CA 2328084	AA	19991111	CA 1999-2328084	19990504	
AU 9938823	A1	19991123	AU 1999-38823	19990504	
EP 1078095	A1	20010228	EP 1999-921681	19990504	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO					
JP 2002513583	T2	20020514	JP 2000-547250	19990504	

PRIORITY APPLN. INFO.: US 1998-73076 A 19980504
WO 1999-US9813 W 19990504

AB The present invention is directed to a method of producing recombinant viral vectors at high titers incorporating a variety of important advancements over the art. The method of the present invention incorporates multiple features which provide enhanced prodn. of viruses, particularly those viruses encoding exogenous transgenes. The specifically illustrated method describes a method for the high titer serum-free media prodn. of recombinant replication defective adenoviruses contg. an exogenous transgene. The invention provides methods of prepg. microcarriers, methods for seeding bioreactors at high cell d., increasing the infectivity of the producer cells to the virus, methods to increase product yield through synchronization of the cell cycle of the producer cells, and methods to minimize the deleterious effects of exogenous transgenes. The invention further provides producer cells prepd. by the process of the invention. The invention further provides viruses produced by the process.

IC ICM C12N015-86
ICS C12M003-00; C12N005-10
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 9, 10, 13, 16
ST transgene **adenovirus** vector prodn microcarrier bioreactor

IT Virus vectors
(recombinant **adenovirus** (ACN53)-based; prodn. of recombinant replication-deficient viral vectors encoding exogenous transgenes via microcarrier-based process)

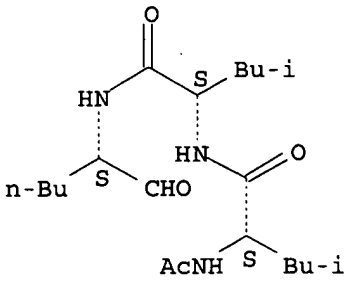
IT Human **adenovirus** 5
(replication defective; prodn. of recombinant replication-deficient viral vectors encoding exogenous transgenes via microcarrier-based process)

IT **110044-82-1**, Calpain inhibitor I
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. of recombinant replication-deficient viral vectors encoding exogenous transgenes via microcarrier-based process)

IT **110044-82-1**, Calpain inhibitor I
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. of recombinant replication-deficient viral vectors encoding exogenous transgenes via microcarrier-based process)

RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:282114 HCAPLUS
DOCUMENT NUMBER: 130:276781
TITLE: Prevention and treatment of adhesion formation by reduction of internalization and degradation of plasminogen activators in mesothelial cells
INVENTOR(S): Kooistra, Teake
PATENT ASSIGNEE(S): Nederlandse Organisatie Voor Toegepast-Natuurwetenschappelijk Onderzoek TNO, Neth.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920297	A1	19990429	WO 1998-NL593	19981015
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1024823	A1	20000809	EP 1998-951807	19981015
EP 1024823	B1	20020508		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001520201	T2	20011030	JP 2000-516693	19981015

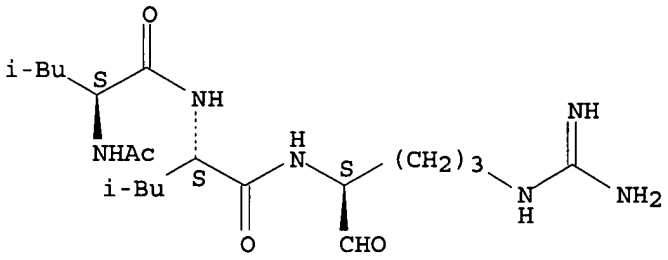
PRIORITY APPLN. INFO.: EP 1997-203217 A 19971016
WO 1998-NL593 W 19981015

AB To reduce or prevent adhesions to or between organs, parts of organs or tissues, at a particular location in a mammal, the invention proposes to subject the mammal to a treatment which provides for reduced internalization and degrdn. of plasminogen activators in mesothelial cells present at the location. In particular, the mammal is treated locally with an active agent capable of interfering with internalization of plasminogen activators by their receptors on mesothelial cells, or interfering with recycling of these receptors, or blocking these receptors to prevent binding of plasminogen activators, or interfering with degrdn. of plasminogen activators in mesothelial cells. Examples of such active agents are chloroquine and 39 kd receptor-assocd. protein. Alternatively, expression of said receptors by the mesothelial cells is downregulated, or the mammal is treated with a plasminogen activator mutant which resists receptor-mediated endocytosis.

IC ICM A61K038-17
ICS A61K031-47; A61K048-00; A61K038-55

CC 1-12 (Pharmacology)
Section cross-reference(s): 63
IT Virus vectors
(**adenovirus**; adhesion prevention and treatment by redn. of internalization and degrdn. of plasminogen activators in mesothelial cells)
IT 54-05-7, Chloroquine 64-86-8, Colchicine 14930-96-2, Cytochalasin B 17090-79-8, Monensin 39324-30-6, Pepstatin **55123-66-5**, Leupeptin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesion prevention and treatment by redn. of internalization and degrdn. of plasminogen activators in mesothelial cells)
IT **55123-66-5**, Leupeptin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesion prevention and treatment by redn. of internalization and degrdn. of plasminogen activators in mesothelial cells)
RN 55123-66-5 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-formylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:330478 HCAPLUS
DOCUMENT NUMBER: 125:48433
TITLE: Inhibition of **adenovirus** infection with protease inhibitors
AUTHOR(S): Sircar, Sucheta; Keyvani-Amineh, Hossein; Weber, Joseph M.
CORPORATE SOURCE: Department of Microbiology, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Quebec, Can.
SOURCE: Antiviral Res. (1996), 30(2,3), 147-153
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of a series of cysteine and serine protease inhibitors was tested on the growth of human adenovirus type 2 in tissue culture. In accordance with the nature of the adenovirus protease, only the cysteine protease inhibitors were effective in significantly reducing the prodn. of infectious virus. Addn. of the inhibitors to the medium 18 h after infection gave IC50 of 30, 40 and 80 nM with N-ethylmaleimide, leupeptin and E64c, resp. Several lines of evidence suggest that inhibition of

infectious virus formation operated through the inhibition of the viral protease rather than cellular toxicity: (a) the yield of phys. particles declined only 4-5-fold, while that of infectious virus declined 3-7 orders of magnitude, (b) these particles contained unprocessed precursor proteins and (c) pulse-chase expts. showed that the inhibitors prevented the efficient processing of viral precursor proteins. We conclude that the cysteine protease inhibitors efficiently depress the formation of infectious adenovirus by inhibiting the viral protease.

CC 1-5 (Pharmacology)

ST **adenovirus** virucide cysteine protease inhibitor

IT Virucides and Virustats
(inhibition of **adenovirus** infection with protease inhibitors)

IT Leupeptins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of **adenovirus** infection with protease inhibitors)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(precursor; inhibition of **adenovirus** infection with protease inhibitors)

IT **Virus**, animal
(**adeno**-, inhibition of **adenovirus** infection with protease inhibitors)

IT 87-51-4, IAA, biological studies 128-53-0, N-Ethylmaleimide 329-98-6, PMSF 9076-44-2, Chymostatin 9078-38-0, Soybean trypsin inhibitor 9087-70-1, Aprotinin **37691-11-5**, Antipain 39324-30-6, Pepstatin 66701-25-5, E64 76684-89-4, E64c 81989-95-9, Cystatin **88191-84-8**, MDL 28170 88321-09-9, E64d
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of **adenovirus** infection with protease inhibitors)

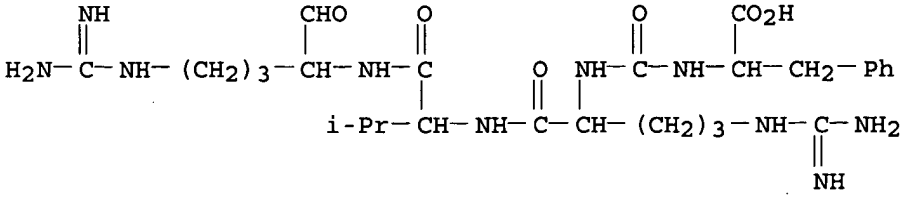
IT 9001-92-7, Protease
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; inhibition of **adenovirus** infection with protease inhibitors)

IT 52-90-4, Cysteine, biological studies 56-45-1, Serine, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(protease inhibitors; inhibition of **adenovirus** infection with protease inhibitors)

IT **37691-11-5**, Antipain **88191-84-8**, MDL 28170
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of **adenovirus** infection with protease inhibitors)

RN 37691-11-5 HCAPLUS

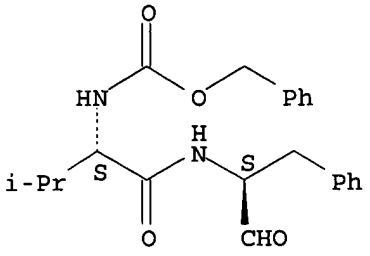
CN L-Valinamide, N2-[[(1-carboxy-2-phenylethyl)amino]carbonyl]-L-arginyl-N-[4-[(aminoiminomethyl)amino]-1-formylbutyl]- (9CI) (CA INDEX NAME)



RN 88191-84-8 HCAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-formyl-2-phenylethyl]amino]carbonyl]-2-methylpropyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:123049 HCAPLUS
DOCUMENT NUMBER: 92:123049
TITLE: Tumor promoters and epidermal growth factor stimulate anchorage-independent growth of **adenovirus** -transformed rat embryo cells
AUTHOR(S): Fisher, Paul Benjamin; Bozzone, Janet H.; Weinstein, I. Bernard
CORPORATE SOURCE: Inst. Cancer Res., Columbia Univ., New York, NY, 10032, USA
SOURCE: Cell (Cambridge, Mass.) (1979), 18(3), 695-705
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of 12-O-tetradecanoylphorbol 13-acetate (I) [16561-29-8], its structural analogs, and epidermal growth factor (EGF) [62229-50-9] on anchorage-independent growth of a cloned population of H5ts 125-transformed rat embryo (RE) cells (clone E11) was studied. Both I and EGF (.apprx.10-8 M) induced a 3-5 fold increase in agar cloning efficiency of E11 cells. In addn., macroscopic colonies appeared earlier and were larger and more diffuse. Phorbol 12,13-didecanoate (PDD) [24928-17-4] and ingenol 3,20-dibenzoate [59086-90-7] also enhanced growth in agar of E11 cells, whereas phorbol [17673-25-5], 4.alpha.PDD [27536-56-7], and 4-O-Me I [16561-29-8] failed to enhance agar growth. In contrast to the results obtained with E11 cells, I, PDD, or ingenol 3,20-dibenzoate failed to induced growth in agar of normal RE cells. Dexamethasone [50-02-2] (10-5-10-6 M), trans-retinoic acid [302-79-4] (10-5-10-6 M) and the protease inhibitors leupeptin, antipain [**37691-11-5**], and elastatinol [59452-67-4] did not inhibit the ability of I to enhance the growth of E11 cells in agar. The I-enhanced anchorage independence was a stable property, since subclones of 11 cells isolated from I-agar plates had a higher agar cloning efficiency than the parental E11 cells when retested in the absence of I. The effect of I did not appear to reflect simple selection of a subpopulation of cells. When the parental E11 cells were 1st cloned in monolayer culture in the absence of I, all 10 randomly picked clones showed enhanced growth in agar in the presence of I. In addn., prior growth of I did not enhance their subsequent growth in agar. The system therefore provides an example in which I appears to enhance the acquisition of a stable cell property, and may be a useful model for studying mechanisms of tumor promotion and progression.

CC 4-7 (Toxicology)
ST phorbol ester **adenovirus** animal cell
IT Leupeptins

RL: BIOL (Biological study)
(phorbol esters enhancement of **adenovirus**-transformed cell growth response to)

IT **Virus**, animal
(**adeno**-, animal cells transformed by, epidermal growth factor and phorbol esters stimulation of growth of)

IT Animal cell
(**adenovirus**-transformed, growth of, epidermal growth factor and phorbol esters stimulation of)

IT 16561-29-8 17673-25-5 24928-17-4 27536-56-7 59086-90-7 62229-50-9
RL: BIOL (Biological study)
(**adenovirus**-transformed cell growth enhanced by, normal cell in relation to)

IT 50-02-2 302-79-4 **37691-11-5** 59452-67-4
RL: BIOL (Biological study)
(phorbol esters enhancement of **adenovirus**-transformed cell growth response to)

IT **37691-11-5**
RL: BIOL (Biological study)
(phorbol esters enhancement of **adenovirus**-transformed cell growth response to)

RN 37691-11-5 HCAPLUS

CN L-Valinamide, N2-[[(1-carboxy-2-phenylethyl)amino]carbonyl]-L-arginyl-N-[4-[(aminoiminomethyl)amino]-1-formylbutyl]- (9CI) (CA INDEX NAME)